|  |  |
| --- | --- |
| **Agenda item:** | **15** |
| **Attachment:** | **J** |

**HRA BOARD COVER SHEET**

|  |  |
| --- | --- |
| **Date of Meeting:** | 16 September 2015 |

|  |  |
| --- | --- |
| **Title of Paper:** | Breach Report - 1 April 2014 - 31 March 2015 |
| **Purpose of Paper:** | For information to the Board |
| **Reason for Submission:** | For information |
| **Details:** | * Details of all breaches reported to the HRA are recorded so that individual breaches can be managed and also to look at themes and trends. * Some key root cause themes have been identified, the need for well planned protocols, the need for good document management systems, the importance of an open an honest reporting culture and ensuring learning not just delivering training. * Analysis of the breaches fed into the work looking to revise the Research Governance Framework. * Further work now being undertaken to inform future learning and improvement in research |
| **Suitable for wider circulation?** | **Yes** |
| **Time required for item:** | **10** |

|  |  |  |  |
| --- | --- | --- | --- |
| **Recommendation / Proposed Actions** | **To Approve** | |  |
| **To Note** | | **x** |
| **For Discussion** | |  |
| **Comments** |  | |

|  |  |
| --- | --- |
| **Name:** | Catherine Blewett |
| **Job Title:** | HRA Improvement & Liaison Manager |
| **Date:** | 14.8.15 |

**Breach Report - UK wide**

**1 April 2014 - 31 March 2015**

**Part 1**

**Introduction**

It is a requirement that all breaches of the standards of good clinical practice or of the study protocol are reported to the reviewing REC for Clinical Trials of Medicinal Products (CTIMPs) (reporting to the MHRA also required), set out in the Medicines for Human Use (Clinical Trial) Regulations 2004. It is also expected that breaches are reported to the REC for non CTIMPs for the purpose of keeping the favourable ethical opinion under review in light of significant developments in the research. Breach notifications are managed centrally by the HRA and classified as a deviation, violation, serious breach, or allegation of fraud or misconduct. All breaches are managed individually but general data is also collected for the purpose of identifying themes and trends to enable the sharing of learning outcomes.

It was recognised that information relating to breaches could be a valuable resource and as a result of this the breach register, which had previously just recorded the breach, was redesigned to capture data fields which can be analysed to identify themes and trends to direct future learning. These data have been collected since April 2013 and have already proved to be valuable. A review of breaches based on these data was undertaken as part of the work looking at the revision of the Research Governance Framework. This work indicated that there were certain commonly occurring themes which may have generalizable solutions such as the ensuring of well planned and well written research protocols and internal procedures from the outset, ensuring effective document management systems and version control, ensuring learning rather than just delivering training and promoting an open and honest reporting culture when things go wrong. Based on these findings, we have also been liaising with the Clinical Research Network, who provide early advice services at the protocol development stage, so that the learning from breaches can be fedback to the early development stages with a view to ensuring that robust protocols and internal processes are imbedded at early stages, to hopefully reduce the number of errors which occur due to poor planning etc. The HRA is also rolling out a function which involves an in-depth review of applications by the REC Manager, before review by the REC, with a view to improving the quality of applications. This supplemented by the HRA assessment may provide the potential for issues which could have led to a breach of the protocol to be picked up and resolved at this stage and for wider learning gained from this work to be fedback to sponsors and researchers for future learning.

Further work being undertaken in relation to breach reporting and management includes reviewing the reporting expectations for non CTIMPs to encourage increased reporting of breaches, in line with the standard of promoting an open and honest reporting culture. The REC and the HRA can provide a supportive function to sponsors, investigators and research organisations when breaches occur and will help to ensure that good quality research proceeds in a way which ensures effective outcomes, whilst also ensuring that participants are protected. We are also undertaking a piece of work to provide a more consistent and effective breach categorisation method so that breaches are managed appropriately and proportionately depending on what has occurred. We are reviewing a number of breaches which have occurred with a view to developing an algorithm, based on various factors such as severity or impact, number of people affected, number of occurrences etc. The purpose of this work is to ensure that the breaches which require urgent intervention and have the highest risk are identified more easily and the lower risk breaches are managed proportionately to ensure effective resource allocation.

The HRA lead on research fraud and misconduct, Dr Frank Wells, has presented the work being undertaken by the HRA at international events and feedback received has been extremely positive and has indicated that this type of work is unique to the UK. Frank was previously a member of the National Research Ethics Advisory Panel (NREAP), is internationally renown for his work on research fraud and misconduct and is the Vice Chair of the Cambridge South REC.

The following data fields are recorded for all breaches notified to the HRA:

1. Whether the notification relates to one or multiple breaches for the same study or more than one study.
2. Whether it was a REC breach
3. Was it a UK or non-UK breach
4. Was recruitment halted
5. (For CTIMPs) Was there an MHRA inspection, either triggered or routine
6. Study details (title, REC reference, EudraCT number etc.)
7. Sponsor, site & Chief Investigator details.
8. How was the breach initially identified
9. Study type (CTIMP or Other)
10. Breach type

**Breach notifications**

The breach notifications received during the reporting period 1 April 2014 - 31 March 2015 are broken down in the following sections:

1. **Breach classification**

|  |  |  |
| --- | --- | --- |
| **Category** | **No.** | **%** |
| Serious breach | 86 | 41.75 |
| Violation | 107 | 51.94 |
| Deviation | 11 | 5.64 |
| Fraud or misconduct | 2 | 0.97 |
| ***Total*** | **206\*** | **100.00** |

**\*As a total of all active research this is expected to be <0.5% of studies**

1. **Type of study**

|  |  |  |
| --- | --- | --- |
| **Study Type** | **No.** | **%** |
| CTIMPs | 147 | 71.36 |
| Other | 59 | 28.64 |
| ***Total*** | **206** | **100.00** |

1. **Other factors**

|  |  |  |
| --- | --- | --- |
| **Factor** | **No.** | **%** |
| Multiple breaches | 9 | 4.37 |
| REC breach | 2 | 0.97 |
| Study halted | 11 | 5.34 |

1. **Type of breach**

|  |  |  |
| --- | --- | --- |
| **Type of breach** | **No.** | **% of total** |
| IMP | 51 | 24.75 |
| Recruitment/informed consent | 75 | 36.41 |
| Record keeping | 11 | 5.34 |
| Safety reporting | 13 | 6.31 |
| No approval (No R&D, substantial amendment not approved, no Clinical Trial Agreement, No REC FO) | 17 | 8.25 |
| Tissue | 6 | 2.91 |
| Data protection | 17 | 8.25 |
| Other | 71 | 34.47 |

**Summary of actions taken by the HRA**

The HRA maintains close liaison with the MHRA in respect of breaches relating to CTIMPs. It follows the lead taken by the MHRA which considers breaches on the basis of their actual impact on patient safety and validity of trial data. Once the MHRA has confirmed that it is satisfied with action taken to protect current and future participants in the trial and to safeguard the integrity of the data, the HRA arranges review of the breach and resultant action taken from an ethical point of view including the potential for the event to reoccur. This generally involves a review by a Sub-Committee of the reviewing REC, which may request further information/action in the interests of participants.

**Examples of further information/action requested by REC**s

* Assurances that adequate action has been taken to rectify the problem and prevent recurrences for future participants in the research
* Confirmation that samples taken improperly have been destroyed.
* Confirmation that an amendment has been submitted and approved to rectify the cause of the breach
* Confirmation that appropriate steps are in place to ensure patient confidentiality
* Reassurances about training, revisions to safety protocols etc

Additional action is taken exceptionally where deemed necessary. For example this may include: requesting that recruitment is suspended until outstanding issues are resolved, suspension of the favourable opinion from the REC or very exceptionally, termination of the favourable opinion.

Note is taken of multiple transgressions, whether occurring at a particular site or in association with a particular individual, and information is shared with the MHRA on such matters where appropriate.

**Position at end of year**

At the end of the year under review, the position of breaches received was as follows:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Open** |  | **Closed** |  |  |  |
| **Type of study** | **No.** | **%** | **No.** | **%** |  | **No.** |
| CTIMPs | 75 | 36.9 | 72 | 35.4 |  | 149 |
| Other | 29 | 14.1 | 28 | 13.6 |  | 57 |
| ***Total*** | **105** | *51.0* | **101** | *49.0* |  | **206** |